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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,497	06/27/2002	John C. Reed	066654-0704	2174

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
09/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,497	REED, JOHN C.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-117* is/are pending in the application.

4a) Of the above claim(s) *111-113 and 115-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-110 and 114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Reed

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/23/07 has been entered.

2. Claims 89-117 are pending. Claims 1-88 are cancelled.

3. Due to species election of BAG-1 (see applicant's response filed on 9/23/05), claims 111-113 and 115-117 are withdrawn from consideration as being drawn to non-elected inventions.

4. Claims 89-110, and 114 are under examination. Claims are examined to the extent that BAG-1 gene encodes BAG-1.

Response to Arguments

5. The rejection of claims 89-110 and 114 under 35 U.S.C. 103(a) as being unpatentable over Froesch et al. (Proceedings of the American Association for Cancer Research Annual Meeting, March, 1998, 89: 13, print) in view of the teachings of Takayama et al. (Cancer Research 1998, 58: 3116-3131, IDS), Noordzij et al. (J.

Urology, 1997, 158: 1880-1885) and Sano et al. (US patent NO. 5,665,539, IDS) is maintained.

The response states that the alleged teaching of Takayama, i.e. "BAG-1 has been shown to increase the metastatic potential of tumor cells *in vivo*" was based on an article by Yawata et al. (Exhibit 1). Yawata et al. report that overexpression of Bcl-2 or BAG-1 enhances peritoneal dissemination of human gastric MKN74 cells in nude mice. In other words, the Takayama et al. alleged teaching should not have been interpreted broader than its source. For a person having ordinary skill in the art and having the capability of appreciating the complexity of scientific issues in cancer, the BAG-1 effects in dissemination of gastric cancer cells in mice could have hardly provided any reasonable expectation of success for that person to want to apply the same concept to prostate cancer in human and coming up with a method of determining the risk of tumor recurrence or spread in patients suffering from prostate cancer, as claimed. The response states that at the time the claimed invention was made, alternative reports in the cancer field taught that BAG-1 expression actually promoted host survival, not cell survival of cancer cells, in patients with early-stage breast cancer or nonsmall cell lung cancer (NSCLC) (Exhibits 2 and 3). Figure 3 of Exhibit 2 showed that high BAG-1 protein level was associated with improved overall survival (OS) and improved distant metastasis-free survival (DMFS) in patients with early-stage breast cancer. Exhibit 3 showed that BAG-1 expression was correlated with overall survival in patients with NSCLC. The response states that Noordzij et al. found no correlation with Bcl-2. As such, a person of ordinary skill in the art would not have been motivated nor have had a

reasonable expectation of success to combine the teachings of Froesch et al. with those of Takayama et al., Noordzij et al. and/or Sano et al. to arrive at the claimed methods.

Applicant's arguments have been carefully considered but are not found persuasive. The Exhibits 1-3 have been carefully reviewed but are insufficient to overcome the rejection. It is noted that Exhibits 2 and 3 are both published after the instant filing date. As such, Exhibits 2 and 3 would not have any input to one skilled in the art at the time the instant invention was made. Regarding Exhibit 1, Yawata et al. teach that prolonged cell survival introduced by overproduction of BAG-1 strongly enhances peritoneal dissemination of human gastric cancer cells (see abstract). Yawata et al. further disclose that overexpression of BAG1 leads to prolonged cell survival of murine melanoma B16 cells, and this enhanced anti-cell death activity promotes their pulmonary metastasis (see page 2682, lines 1-3). With respect to the state of the prior art, Tang et al. (J. Clin. Oncology, 1999, June, 17(6): 1710-1719, IDS) teach that BAG-1 is overexpressed in the majority of invasive breast carcinomas, and its overexpression may be associated with a shorter disease-free and overall survival (see abstract, Figures 3 and 4). Tang et al. teach that overexpression of BAG-1 resulted in sustained cell viability and proliferation with minimal apoptosis and a growth factor-independent state (see page 1711, 2nd paragraph, lines 7-10). Tang et al. disclose that patients whose tumors expressed BAG-1 tended to have less favorable clinical outcome (see page 1716, last paragraph). Yang et al. (Exp. Cell Res. 1999, Feb., 247: 200-207, IDS) teach that overexpression of BAG1 enhanced the resistance of cervical cells to apoptosis and may play an important role in apoptosis and human cervical

carcinogenesis (see abstract). Takayama et al. teach that overexpression of BAG-1 has been shown to increase the metastatic potential of tumor cells *in vivo* (see page 3116, right column, 2nd paragraph, lines 5-7). Takayama et al. teach that BAG-1 can promote cell survival and augment the bioactivities of several proteins known to be important for tumorigenesis (e.g. bcl-2, Raf-1, HGF-R, and PDGF-R) (see page 3117, left column, 3rd paragraph). Takayama et al. teach that BAG-1 can be regarded as a candidate proto-oncogene (see page 3117, left column, 3rd paragraph). Takayama et al. teach that BAG-1 protein is consistently the most abundant form of BAG-1 expressed in tumors (see page 3127, left column, 1st paragraph). Therefore, in view of the teachings of prior art such as Yawata, Tang, Yang, and Takayama, one of ordinary skill of art would reasonable conclude that the overexpression of BAG-1 protein promotes the cancer cell survival and is correlated with the metastatic potential of tumor cells. Froesch et al. teach that BAG-1 protein (cytosolic BAG protein) is expressed in all 9/9 prostate cancer cell lines and 51/51 archival prostate tumor specimens (see abstract and title). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to determine the level of BAG-1 expressed in prostate cancer using immuno-PCR, compare the level with a reference level and further correlate the results with the risk of tumor recurrence, tumor spread and survival in a patient suffering from prostate cancer in view of the teachings of Froesch, Takayama, Noordzij and Sano. One would have been motivated to do so because Froesch et al. teach that BAG-1 protein is expressed in all 9/9 prostate cancer cell lines and all 51/51 prostate tumor specimens, and Takayama teaches that overexpression of

BAG-1 has been shown to increase the metastatic potential of tumor cells in vivo and BAG-1 promotes cell survival. Moreover, one of ordinary skill in the art would have had a reasonable expectation of success to determine the level of BAG-1 protein expressed in prostate cancer using immuno-PCR, compare the level with a reference level and further correlate the results with the risk of tumor recurrence, tumor spread and survival in a patient suffering from prostate cancer because Froesch et al have already successfully detected BAG-1 protein in all 9/9 prostate cancer cell lines and all 51/51 prostate tumor specimens, and Takayama teaches that overexpression of BAG-1 has been shown to increase the metastatic potential of tumor cells in vivo, and BAG-1 protein promotes cell survival. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Because of these reasons, the rejection is maintained.

Conclusion

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Sept. 4, 2007

/Christopher Yaen/
Primary Examiner
Art Unit 1643
September 13, 2007